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(FILE 'HOME' ENTERED AT 15:27:50 ON 17 DEC 2007)

FILE 'REGISTRY' ENTERED AT 15:28:00 ON 17 DEC 2007 STRUCTURE UPLOADED L1

FILE 'STNGUIDE' ENTERED AT 15:28:51 ON 17 DEC 2007

FILE 'REGISTRY' ENTERED AT 15:32:17 ON 17 DEC 2007

L2 STRUCTURE UPLOADED

1 S L2 L3

L45 S L2 SSS FULL

FILE 'HCAPLUS' ENTERED AT 15:33:47 ON 17 DEC 2007

L53 S L4

L6 3 S ABBOTT, F?/AU AND KARAGIOZOV, S?/AU

L7 3996 S VALPROIC (A) ACID

2 S FLUORINATED (A) VALPROIC (A) ACID L8

FILE 'STNGUIDE' ENTERED AT 15:38:46 ON 17 DEC 2007

FILE 'HCAPLUS' ENTERED AT 15:44:27 ON 17 DEC 2007

L9 0 S "VPA OR VALPROIC (A) ACID" (S) "FLUORINE OR FLUORINATE OR FLU L10

0 S "VPA OR VALPROIC (A) ACID" (5N) "FLUORINE OR FLUORINATE OR FL

STS Connecting via Winsock to Welcome to STN International! Enter x:x

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ERMINAL (ENTER 1, 2, 3, OR ?):2

Welcome to STN International * * * * * * * * *

Web Page for STN Seminar Schedule - N. America ASA REGISTRY enhanced with new experimental property tags FSTA enhanced with new thesaurus edition CA/CAplus enhanced with additional kind codes for granted AUG 06 AUG 06 AUG 13 NEWS NEWS

AUG 20 AUG 27 s o

patents
CA/CAplus enhanced with CAS indexing in pre-1907 records
CA/CAplus enhanced with catabases enhanced with predefined
patent family display formats from INPADOCDB
USPATOLD now available on STN
CAS REGISTRY enhanced with additional experimental AUG 27 AUG 28 œ NEWS NEWS

NEWS 9 SEP 07

13 13 SEP SEP SEP NEWS 10 NEWS 11 NEWS 12

CAplus coverage extended to include traditional medicine patents EMBASE, EMBAL, and LEMBASE reloaded with enhancements SEP 17 24 SEP NEWS 13

BEILSTEIN updated with new compounds
Derwent Indian patent publication number format enhanced
WPIX enhanced with XML display format
ICSD reloaded with enhancements CA/CAplus enhanced with pre-1907 records from Chemisches Zentralblatt NEWS 14 NEWS 15

IMSDRUGCONF removed from database clusters and STN DGENE now includes more than 10 million sequences TOXCENTER enhanced with 2008 MeSH vocabulary in LINPADOCDB now available on STN BELLSTEIN pricing structure to change USPATOLD added to additional database clusters OCT 19 NOV 15 NOV 19 NOV 30 DEC 04 DEC 17 DEC 17 DEC 17 DEC 17 NEWS 16
NEWS 17
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MEDLINE segment was an in 2008 meSH vocabulary MEDLINE undated with 2008 meSH vocabulary CA/CAplus enhanced with new custom IPC display formats STN Viewer enhanced with full-text patent content DEC 17 DEC 17 DEC 17 NEWS 26 NEWS 27 NEWS 28

19 SEPTEMBER 2007: CURRENT WINDOWS VERSION IS V8.2, CURRENT MACINTOSH VERSION IS V6.0C(ENG) AND V6.0JC(JP), AND CURRENT DISCOVER FILE IS DATED 19 SEPTEMBER 2007. NEWS EXPRESS

STN Operating Hours Plus Help Desk Availability NEWS HOURS

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10/539049 VALPROIC ACID ANALOGUES

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Columbus * * * * * * * * * * * * * * * NLS * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 15:27:50 ON 17 DEC 2007

TOTAL SESSION 0.21 SINCE FILE ENTRY 0.21 => file reg COST IN U.S. DOLLARS FULL ESTIMATED COST

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

HIGHEST RN 958294-65-0 HIGHEST RN 958294-65-0 16 DEC 2007 16 DEC 2007 STRUCTURE FILE UPDATES: DICTIONARY FILE UPDATES: New CAS Information Use Policies, enter HELP USAGETERMS for details

TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

Please note that search-term pricing does apply when conducting SmartSELECT searches. REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=> Uploading C:\Program Files\Stnexp\Queries\2007cases\10539049\formula1.str

Page 2 12/17/07

7-8 8-9 chain nodes:
1 2 3 4 5 6 7 8 9 10 16
1 2 3 4 5 6 7 8 9 10 16
chain bonds:
1-2 2-3 2-6 2-16 3-4 4-5 5-10 6-7 7exact/norm bonds:
2-3 2-6 2-16 3-4 5-10 6-7 8-9
exact bonds:
1-2 4-5 7-8

G1:F,H

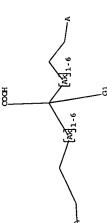
Connectivity:

3:2 M uinimum RC ring/chain 6:2 M uinimum RC ring/chain Marchi Level : 1:CLASS 2:CLASS 3:CLASS 4:CLASS 5:CLASS 6:CLASS 7:CLASS 8:CLASS 9:CLASS 10:CLASS 16:CLASS

STRUCTURE UPLOADED Ę

=> d ll L1 HAS NO ANSWERS L1 STR

10/539049 VALPROIC ACID ANALOGUES



G1 F,H

Structure attributes must be viewed using STN Express query preparation.

a> 9 11 GENERIC GROUP NOT VALID HERE Generic groups may not be used in these circumstances:

Any generic group node (e.g., Hy) in a ring.
 An Ak node attached to another Ak node.
 An Ak node with three or more attachments where one or more of the attachments is to a C node.

SINCE FILE ENTRY 0.45 => fil stng cost in U.S. DOLLARS FULL ESTIMATED COST

FILE 'STNGUIDE' ENTERED AT 15:28:51 ON 17 DEC 2007 USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

FILE CONTAINS CURRENT INFORMATION. LAST RELOADED: Dec 14, 2007 (20071214/UP).

TOTAL SESSION 1.02 SINCE FILE ENTRY 0.36 => file reg
cost IN U.S. DOLLARS FULL ESTIMATED COST

FILE 'REGISTRY' ENTERED AT 15:12:17 ON 17 DEC 2007
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 16 DEC 2007 HIGHEST RN 958294-65-0 DICTIONARY FILE UPDATES: 16 DEC 2007 HIGHEST RN 958294-65-0

New CAS Information Use Policies, enter HELP USAGETERMS for details.

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Page 3 12/17/07

ISCA INFORMATION NOW CURRENT THROUGH June 29, 2007

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http://www.cas.org/support/stngen/stndoc/properties.html

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chain nodes:
1 2 3 4 5 6 7 8 9 10 16 18
1-2 3 4 5 6 7 8 9 10 16 18
1-2 1-3 2-6 2-16 3-4 4-5 5-10 6-7 7-8 8-9
exact/norm bonds:
2-16 5-10 8-9
exact bonds:
1-2 2-3 2-6 3-4 4-5 6-7 7-8

G1:F,H

G2:F,H

Match level : 1:CLASS 2:CLASS 3:CLASS 4:CLASS 5:CLASS 6:CLASS 7:CLASS 8:CLASS 9:CLASS 10:CLASS 16:CLASS 18:CLASS

STRUCTURE UPLOADED

S

Page 5 12/17/07

10/539049 VALPROIC ACID ANALOGUES

=> d l2 L2 HAS NO ANSWERS L2 STR

G1 F,H

G2 F,H

Structure attributes must be viewed using STN Express query preparation.

=> \$ 12 SAMPLE SEARCH INITIATED 15:32:39 FILE 'REGISTRY' SAMPLE SCREEN SEARCH COMPLETED - 444 TO ITERATE

100.0% PROCESSED 444 ITERATIONS SEARCH TIME: 00.00.01

1 ANSWERS

10144 FULL FILE PROJECTIONS: ONLINE **COMPLETE**
PROJECTED ITERATIONS: 7016 TO 1014
PROJECTED ANSWERS: 1 TO 8

1 SEA SSS SAM L2 L3

=> d sca

L3 1 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN
IN Octanicla caid, 2,3,4,4,5,5,6,6,7,7,8,8,8-tetradecafluoro-2(nonafluorobutyl)-, ammonium salt (9CI)
MF C12 H F23 02 - H3 N

F3C- (CF2) 3-C- (CF2) 5-CF3

● NH₃

Page 6 12/17/07

ALL ANSWERS HAVE BEEN SCANNED

> 9 12 858 full FULL SEARCH INITIATED 15:33:04 FILE 'REGISTRY' FULL SCREEN SEARCH COMPLETED - 7817 TO ITERATE

2 INCOMPLETE) 100.0% PROCESSED 7817 ITERATIONS (SEARCH TIME: 00.00.03

5 SEA SSS FUL L2

7

=> d scan 1-5 ide '1-5' IS NOT A VALID FORMAT FOR FILE 'REGISTRY'

5 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

ITERATION INCOMPLETE
Propanedioic acid, bis(heptadecafluorooctyl)-(9CI)
CON 12 F34 O4

C # I

C- (CF2) 7-CF3 P3C- (CF2) 7**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT **

The following are valid formats:

Substance information can be displayed by requesting individual fields or predefined formats. The predefined substance formats are: (RN = CAS Registry Number)

REG - RN
SAM - Index Name, MF, and structure - no RN
FIDE - All substance data, except sequence data
IDE - FIDE, but only 50 names
SQIDE - IDE, plus sequence data
SQIDE - Protein sequence data, includes RN
SQD - Protein sequence data, includes RN
SQD - Same as SQD, but 3-letter amino acid codes are used
SQD - Same as SQD, and 3-letter amino acid codes are used
SQN - Protein sequence name information, includes RN

CALC EPROP PROP

Table of calculated properties
 Table of experimental properties
 EPROP and CALC

Any CA File format may be combined with any substance format to obtain CA references citing the substance. The substance formats must be cited first. The CA File predefined formats are:

Page 7 12/17/07

10/539049 VALPROIC ACID ANALOGUES

ABS -- Abstract
APPS -- Application and Priority Information
BIB -- CA Accession Number, plus Bibliographic Data
CAN -- CA Accession Number
CBIB -- CA Accession Number,
IND -- Index Data
IND -- Index Data
IPC -- Infernational Patent Classification
PATS -- PI, SO
STD -- BIB, IPC, and NCL

IABS -- ABS, indented, with text labels IBIB -- BIB, indented, with text labels ISTD -- STD format, indented

OBIB ----- AN, plus Bibliographic Data (original) OIBIB ----- OBIB, indented with text labels

SBIB ----- BIB, no citations SIBIB ----- IBIB, no citations

The ALL format gives FIDE BIB ABS IND RE, plus sequence data when

it is available. The MAX format is the same as ALL. The IALL format is the same as ALL with BIB ABS and IND indented,

with text labels.

For additional information, please consult the following help

messages:

HELP DFIELDS -- To see a complete list of individual display fields. HELP FORMATS -- To see detailed descriptions of the predefined formats. HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):5

Octanoic acid, 2,3,3,4,4,5,5,6,6,7,7,8,8,8-tetradecafluoro-2-(nonafluorobutyl)-, ammonium salt (9CI) 7 Z

Ě

F3C- (CF2) 3- C- (CF2) 5-CF3

● NH3

5 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN Nonanoic acid, 2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,9-hexadecafluoro-2-(heptafluoropropyl) - (9Cl) C12 H F23 O2 1 L

Ψ

Page 8 12/17/07

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN TETRATION INCOMPLETS Propanedioic acid, bis(heptadecafluorooctyl)-,disodium salt (9CI) C19 H2 F34 04 .2 Na A I E

$$F_3 C - (CF_2) 7 - C - (CF_2) 7 - CF_3$$

$$CO_2 H$$

Š ² 5 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN
Octanoic acid, 2,3,3,4,4,5,5,6,6,7,7,8,8,8-tetradecafluoro-2(nonafluorobutyl) - (9CI)
CL2 H F23 O2
COM C A 7 Z

F3C- (CF2) 3- Ç- (CF2) 5- CF3

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

ALL ANSWERS HAVE BEEN SCANNED

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(FILE 'HOME' ENTERED AT 15:27:50 ON 17 DEC 2007)

FILE 'REGISTRY' ENTERED AT 15:28:00 ON 17 DEC 2007 STRUCTURE UPLOADED ដ

Page 9 12/17/07

10/539049 VALPROIC ACID ANALOGUES

FILE 'STNGUIDE' ENTERED AT 15:28:51 ON 17 DEC 2007

FILE 'REGISTRY' ENTERED AT 15:32:17 ON 17 DEC 2007 STRUCTURE UPLOADED

252

1 S L2 5 S L2 SSS FULL

=> fil hcapl COST IN U.S. DOLLARS

SINCE FILE ENTRY 173.00 FULL ESTIMATED COST

TOTAL SESSION 174.02

FILE 'HCAPLUS' ENTERED AT 15:33:47 ON 17 DEC 2007
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FILE COVERS 1907 - 17 Dec 2007 VOL 147 ISS 26 FILE LAST UPDATED: 14 Dec 2007 (20071214/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

a> 8 14 L5

3 L4

=> d l5 1-3 ibib abs hitstr

L5 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2007 ACS ON STN ACCESSION NUMBER: 1998:323285 HCAPLUS DOCUMENT NUMBER: 129:16513

Aqueous fluoropolymer compositions and their preparing methods TITLE:

INVENTOR(S):

Fan, Wei-qiang; Manzara, Anthony P. Minnesota Mining and Manufacturing Co., USA PCT int. Appl., 79 pp. CODEN: PIXXES

PATENT ASSIGNEE(S): SOURCE:

Patent English LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION: DOCUMENT TYPE:

19970319 WO 1997-US4446 APPLICATION NO. 19980514 DATE KIND WO 9820055 PATENT NO.

Page 10 12/17/07

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DE,
KZ,
VN, YU
GB,
GN,
                                    19961104
19970319
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19990430
19961104
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CI BAY, CI
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                                    1996-743573
11997-22184
1997-915175
                                                              CN 1997-180208
JP 1998-521343
KR 1999-703836
US 1996-743573
WO 1997-US446
BY, CA,
IS, JP,
MK, MN,
TM, TR,
CH, DE,
BJ, CF,
BR,
IL,
TJ,
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AU
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A 19990818
B1 20011128
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FR, IT, LI NL
A 19991222
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GE, GH,
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CN 1239483
JP 2001503801
KR 2000052962
PRIORITY APPLN: INFO::
AM,
LK,
KB,
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PT.
                                    US 5998521
AU 9722184
EP 935621
EP 935621
                      RW:
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MARPAT 129:16513 SOURCE (S): OTHER AB T

The compns. comprise fluoropolymers, and 21 environmentally-friendly fluorinated emulsifier comprising u-branched fluoropolymers are selected from PTFE fluoroalkylarbonylmoieties. The fluoropolymers are selected from PTFE or polyvinylidene fluoride. Methods for preparation of intermediates, monomers, repellent treatments, coatings, surfactants, emulsifiers, and aqueous film-forming foamable solns. are included.
20779-54-4P 207678-57-7P 207678-73-7P.
RL: IMF (Industrial manufacture), FRP (Properties); PREP (Preparation) (aqueous fluoropolymer compns. containing environmentally-friendly

H

emulsifiers) fluorinated

<u>8</u> 8

207678-54-4 HGAPLUS Nonanoic acid, 2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,9-hexadecafluoro-2-(heptafluoropropyl)-(9CI) (CA INDEX NAME)

F3C-CF2-CF2-C-CF2)6-CF3 82H

207678-57-7 HCAPLUS Octanoic acid, 2,3,3,4,4,5,5,6,6,7,7,8,8,8-tetradecafluoro-2-(nonafluorobuty1)-(9CI) (CA INDEX NAME) ₹ ₹

F3C- (CF2) 3- Ç- (CF2) 5- CF3

207678-73-7 HCAPLUS
Octanoia acid, 2,334,4,5,5,6,6,7,7,8,8,8-tetradecafluoro-2(nonafluoroburyl)-, ammonium salt (9c1) (CA INDEX NAME) ₹ §

Page 11 12/17/07

10/539049 VALPROIC ACID ANALOGUES

C- (CF2) 5- CF3 F3C- (CF2) 3-

● NH3

THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT REFERENCE COUNT:

CAPLUS COPYRIGHT 2007 ACS on STN
1998:323170 HCAPLUS
129:17563
Aqueous film-forming foam compositions
Stern, Richard M.; Fan, Wei-qiang
Minnesota Mining and Manufacturing Co., USA
PCT Int. Appl., 81 pp.
PCT Int. Appl., 81 pp.
Patent
Baglish HCAPLUS LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION: LS ANSWER 2 OF 3 H ACCESSION NUMBER: DOCUMENT NUMBER: TITLE: INVENTOR(S): PATENT ASSIGNEE(S): SOURCE: DOCUMENT TYPE:

| PATENT NO. | | | KIND | | DATE | | 4 | IPPL | APPLICATION NO. | ION | ō. | | ā | DATE | | |
|------------------------|------|-----|------|-----|----------|------------------|------|------|-----------------|---------|-----|-----|-----|-------------|-----|---|
| WO 9819742 | | | A1 | , | 19980514 | 514 | ۰ .> | Ş | WO 1997-US4560 | 0845 | 60 | | . 1 | 19970318 | 318 | |
| W: AL, | | | | AZ, | BA, | BB, | BG, | BR, | ВУ, | ð | Ŗ | 5 | S, | CZ, | DE, | |
| DK, | | | | g, | GE, | Ħ, | HG, | ï. | IS, | JP, | Ä | χĠ, | 8 | Ř, | ğ | |
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| RW: GH, | | | | S, | SZ, | ng, | AT, | BE, | Ð | DE, | DK, | ES, | F, | FR, | g, | |
| gR, | IE, | Ë | ΓΩ, | MC, | NF, | Ч, | SE, | BF, | BF, BJ, C | GF. 83, | 8 | G, | ₹ | CM, GA, GN, | Š | |
| ML, | | | | 5 | ŢĠ | | | | | | | | | | | |
| US 6015838 | | | Æ | | 20000118 | 118 | _ | 35 1 | -966 | 7434 | 78 | | - | 19961101 | 101 | |
| CA 2269340 | | | A1 | | 19980514 | 514 | Ŭ | 1 | CA 1997-2269340 | 2269 | 340 | | - | 19970318 | 318 | |
| | | | Ø | | 19980529 | 5229 | ~ | 10 | 1997-25854 | 2585 | 4 | | - | 19970318 | 318 | |
| AU 723935 | | | B2 | | 2000002 | 7060 | | | | | | | | | | |
| EP 935486 | | | A1 | | 19990818 | 3818 | щ | 면 | EP 1997-917568 | 9175 | 89 | | - | 19970318 | 318 | |
| EP 935486 | | | B1 | | 20011017 | 1017 | | | | | | | | | | |
| R: BE, | H, | DE, | FR, | g, | IT, | GB, IT, LI, NL | Ν̈́ | | | | | | | | | |
| CN 1239897 | | | Ø | | 19991229 | 1229 | Ŭ | 7 | 1997-180300 | 1803 | 00 | | - | 19970318 | 318 | |
| JP 2002514240 | 40 | | ۲ | | 20020514 | 0514 | ٠, | 1P 1 | 1998-521344 | 5213 | 44 | | - | 19970318 | 318 | |
| KR 2000052963 | 63 | | Ø | | 20000825 | 3825 | _ | KR 1 | 1999-703837 | 7038 | 37 | | - | 19990430 | 430 | |
| PRIORITY APPLN. INFO.: | INFO | •; | | | | | _ | US 1 | 1996-743478 | 7434 | 78 | _ | 4 | 19961104 | 104 | |
| | | | | | | | _ | WO 1 | 1997-US4560 | US45 | 9 | _ | 7 | 9970 | 318 | |
| OTHER SOURCE(S): | | | MAR | PAT | 129: | MARPAT 129:17563 | _ | | | | | | | | | |

A SOURCE (S): This invention provides aqueous film-forming foamable (AFFF) compns. comprising one or more environmentally-friendlyn-branched OTHER AB T

fluoroalkylcarbonyl group-containing surfactants. H

RL: TEM (Technical or engineered material use); USES (Uses) (surfactants, aqueous film-forming foam compns. containing) 207678-54-4 HGAPLUS Nonanoic acid, 2,3,4,4,5,5,6,6,7,7,8,8,9,9,9-hexadecafluoro-2-₹ §

12/11/01 12 Page

(heptafluoropropyl) - (9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT S

Electrostatographictoners
Kato, Koichi, Tomita, Masami; Hagiwara, Tomoe
Klichh Co., Ltd., Japan
Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
Patent LUS COPYRIGHT 2007 ACS on STN 1992:72287 HCAPLUS 116:72287 LS ANSWER 3 OF 3 HCAPLUS ACCESSION NUMBER: 1993 INVENTOR(S): PATENT ASSIGNEE(S): DOCUMENT NUMBER SOURCE:

Japanese LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION: DOCUMENT TYPE:

PRIORITY APPLN. INFO.:

By 1989-316551 A1 19891207

AB The toners consist of binder, coloring agent, and F-containing compound RIR2R32(CF3) MCR465R6 [R1.6 = F, CO2H, COZNH, COZCHZD-1 (P2.1), COZL, COZUH4, SOZNH, SOZNH, COZCHZD-1 NH, NMB31; number of F in R1-654; m22]. The F-containing compound may be CF3(CF2) kCP2CR7R8P8 [R7-9 = as defined for R1-6 or CF3(CP2) (q22); number of F in R7-9 ≤2; k ≥2]. These toners do not form films on sleeves or on photoconductors, and do not produce fog in image.

IT 138707-62-7 138707-64-9 19900912 JP 1990-239980 JP 1989-316551 APPLICATION NO 19911002 DATE KIND A JP 03223767 PATENT NO.

RL: TEM (Technical or engineered material use); USES (Uses) (electrophotog, toner containing, for prevention of film formation and fog) 138707-62-7 HCAPLUS

Propanedioic acid, bis(heptadecafluorooctyl)-, disodium salt (9CI)

3 3

F3C- (CF2) 7- ¢- (CF2) 7- CF3

o 2 Na

Z Z

138707-64-9 HCAPLUS Propanedioic acid, bis(heptadecafluorooctyl)-(9CI) (CA INDEX NAME)

Page 13 12/17/07

10/539049 VALPROIC ACID ANALOGUES

F3C- (CF2) 7- C- (CF2) 7- CF3

=> s abbort,f?/au and karagiozov,s?/au 17 ABBOTT,F?/AU 6 KRAGIOZOV,S?/AU L6 3 ABBOTT,F?/AU AND KARAGIOZOV,S?/AU

=> d 16 1-3 ibib abs

L6 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2007 ACS ON STN ACCESSION NUMBER: 2005:415182 HCAPLUS DOCUMENT NUMBER: 143:146535

Valproic acid glucuronidation is associated with increases in 15-F2t-16oprostane in rate Trong, Vincent, Teng, Xiao Wei, Karagiozov, Stoyan; Chang, Thomas K. H.; Abbott, Frank

AUTHOR(S):

Faculty of Pharmaceutical Sciences, The University of British Columbia, Vancouver, BC, V6T 123, Can. Free Radical Biology & Medicine (2005), 38(11), 1471-1481. FRBMEH; ISSN: 0891-5849 Elsevier CORPORATE SOURCE:

SOURCE:

English Journal PUBLISHER: DOCUMENT TYPE: LANGUAGE: AB Oxidative

rates and studies are organing to examine the relationship between VPA biotransformation and the increase in the lipid peroxidn. biomarker is rate and studies are organing to examine the relationship between VPA biotransformation and the increase in the lipid peroxidn. biomarker 15-F2L-isoprostane (15-F2L-isop). This study investigated the effects of modulating VPA-1-O-acyl glucuronide (VPA-0) formation on 15-F2L-1sop levels. Adult male Sprague-Dawley rate were pretreated with phenobarbical (PB; 80 mg/kg/day for 4 days). (-)-borneol (320 mg/kg). or a combination of both before VPA treatment (500 mg/kg). Liver VPA-0 levels were determined by LC/MS and plasma and liver 15-F2L-1sop levels were measured using an EIA method. PB, an inducer of VPA glucuronidation, elevated both liver VPA-0 and plasma and liver 15-F2L-1sop levels in VPA-treated rate. (-)-Borneol, an inhibitor of glucuronidation, significantly reduced the levels of liver VPA-0 and decreased plasma and liver 15-F2L-1sop levels in both the VPA and the PB + VPA groups. (-)-Borneol and PB alone did not elevate 15-F2L-1sop levels of the vehicle control groups. The fluorinated analog of VPA, "Litoro-VPA, was a poor substrate for glucuronidation and did not elevate 15-F2L-1soP levels. In summary, the VPA-ninduced formation of 15-F2L-1soP levels. In summary, the Oxidative stress has been associated with valproic acid (VPA) treatment in

THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT 98 glucuronidation. REFERENCE COUNT:

L6 ANSWER 2 OF 3 F ACCESSION NUMBER: DOCUMENT NUMBER: TITLE:

HCAPLUS COPYRIGHT 2007 ACS on STN 2004:534162 HCAPLUS 141:65128 Valproic acid analogs, their preparation, and

Page 14 12/17/07

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Analogs of valproic acid useful in treating neuroaffective disorders, including convulsions, bipolar disorder, and migratine headache, are disclosed. The analogs are halide-substituted analogs, cyclic analogs, and conjugated diene analogs of valproic acid. Pharmaceutical compns, or prodrugs contraining the analogs or pharmaceutically acceptable salts thereof are disclosed. Methods of making the compds, and treating mammals with neuroaffective disorders are also disclosed.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Faculty of Pharmaceutical Sciences, Division of Biomolecular and Pharmaceutical Chemistry, University of British Columbia, Vancouver, Vancouver, BC, Can. Synthetic Communications (2004), 34(5), 871-888 CODEN: SYNCAV, ISSN: 0039-7911
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Practical Stereoselective Synthesis of (2E)- and
pharmaceutical compositions and therapeutic use
thereof
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(E)-RICR2:CHCH:CHCO2Et[RIR2 = (CH2)4, (CH2)5, (CH2)6, (CH2)7] and
(Z)-RICR2:CHCH:CHCO2Et[same RIR2] was achieved through
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KR,
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                    Abbott, Frank Slade; Karagiozov, Stoyan Kostadinov
The University of British Columbia, Can.
PCT Int. Appl., 84 pp.
CODEN: PIXXD2
Patent
English
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SL, SZ, TU, UG, ZI
BB, BG, CH, CY, CC
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CA 2003-2508855
AU 2003-289782
US 2002-433505P
WO 2003-CA1960
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PATENT INFORMATION:
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US 2006223888
PRIORITY APPLN. INFO.:
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                                               PATENT ASSIGNEE(S):
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12/11/01 13 Page

10/539049 VALPROIC ACID ANALOGUES

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Horner-Wadsworth-Emmonsreaction of B, B-disubstituted
a, B-unsatd. aldehydes RLCR2:(HCMO (1). Thus, aldehydes In
undergo olefination with phosphonate carbanion generated from tri-Et
blosphonoacetate and lithium hydroxide or Bu lithium/DMPU to give
(E) a, B-unsatd. esters with excellent selectivity. The
treatment of I with the new Horner-Emmons reagents, Et
(diphenylphosphono) acetateand Et (di-o-colyl-phosphono) acetatein the
presence of benzyltrimethyl amenium hydroxide (Triton B) afforded
(Z) -u. B-unsatd. esters with 73-99* selectivity. The esters
were converted to (2E) - and (2Z) -4-cycloalkylidenebut-2-enoicacids.

REFERRNCE COUNT:
10 THERE ARB 10 CITED REFERRNCES AVAILABLE FOR THIS
REFERRNCE COUNT:
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VALPROIC (A) ACID (FLUORINATED OR FLUORINATEDS) s fluorinated (a) valproic (a) acid 3996 VALPROIC (A) ACID (ACID OR ACIDS) (ACID OR ACIDS)
2 FLUORINATED (A) 38949 FLUORINATED
1 FLUORINATEDS 38949 FLUORINATED => s valproic (a) acid 3998 VALPROIC 4498412 ACID 1605681 ACIDS 5004418 ACID 3998 VALPROIC 4498412 ACID 1605681 ACIDS 5004418 ACID ٨ 17 L8

=> d l8 1-2 ibib abs hitstr

valproic acid in mouse brain and serum and its effect on synaptosomal r-aminobutyric acid levels in comparison to valproic acid ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2007 ACS on STN SSION NUMBER: 1997:645639 HCAPLUS MENT NUMBER: 127:314376 Time course of a. fluorinated ACCESSION NUMBER: DOCUMENT NUMBER: TITLE: AUTHOR (S)

CORPORATE SOURCE:

Tang, Wei; Palaty, Jan; Abbott, Frank S.
Division of Pharmaceutical Chemistry, Faculty of
Pharmaceutical Sciences University of British
Columbia, Vancouver, BC, V6T 123, Can.
Journal of Pharmacology and Experimental Therapeutics
(1997), 282(3), 1163-1172
CODEN: JPETAB; ISSN: 0022-3565
Williams & Wilkins

Vorevent the hepatotoxicity of valproic acid (VPA), a fluorine substituent was introduced at the u-position to eliminate the cornation of putative toxic metabolites through mitochondrial \$\theta\$-oxidentialed Although the u-fluorinated VPA analog (u-fluoro VPA) is more acidic (PKa = 3.55) than VPA (PKa = 4.80), the lipophilicity English LANGUAGE: AB To pro

Journal

DOCUMENT TYPE:

PUBLI SHER:

SOURCE:

12/11/01 Page 16

of these two compds., as determined by their log P values, were similar when compared at pH 2.5. Brain, serum and urine samples were prepared from mature male CD-1 mice treated with either u-fluoro VPA or VPA for quantitation of drug concns. Brain synaptosomes were isolated to determine y-aminoburyric acid levels. After equivalent doses of 0.83 mmol/kg, u-fluoro VPA was characterized by its slower access into mouse brain, compared to VPA. The peak concentration of u-fluoro VPA in mouse brain was achieved 45 min later than in the serum, whereas the peak brain level of VPA coincided with the peak serum level occurring within 15 min. Simultaneous curve fitting of both brain and serum drug concns. using a two-compartment model indicated that u-fluoro VPA, like VPA, may be asym. transported across the blood-brain-barrier. This property of u-fluoro VPA was also reflected in its low brain-to-serum concentration ratio of 0.09 at the peak brain drug concentration (0.16 for VPA). The primary p-oxilation metabolite of VPA was not found in the serum and urine of mice treated with u-fluoro VPA. Although the glucuronide was a major metabolite of VPA (28.5% of the dose), u-fluoro VPA was observed to conjugate extensively with L-glucamine (33.3% of the dose).

u-Fluoro VPA appeared to persist in the general circulation, which, in turn, may contribute to the apparent slow elimination of the drug from the brain. The fluorizated compound was demonstrated to have anticonvulsant activity in the 1.5-pentamethyleneterazoleseizure test and to be capable of increasing brain synaptic y-aminobutyric acid, the EDSO being as a new anticonvulsant drug.
REFERENCE COUNT: 58 THE

THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

APDUS COPYRIGHT 2007 ACS on STN 1992:214009 HCAPLUS 116:214009 Treparation of fluorinated valproic acid and anticonvalsants containing them Yamaguchi, Koji; Yanaka, Mikiro Kureha Chemical Industry Co., Ltd., Japan Jpn. Kokai Tokkyo Koho, 8 pp. Japanese HCAPLUS FAMILY ACC. NUM. COUNT: PATENT INFORMATION: L8 ANSWER 2 OF 2 ACCESSION NUMBER: DOCUMENT NUMBER: INVENTOR(S): PATENT ASSIGNEE(S) DOCUMENT TYPE: LANGUAGE: SOURCE:

19900511 DATE JP 1990-122641 APPLICATION NO. 19920124 DATE KIND A B2 JP 04021652 PATENT NO.

PRIORITY APPLA. INFO::

MARRAT 116:214009

RECREG(S):

MARRAT 116:214009

MARRA Oral administration of I Na salt at 1320 mg/kg (4.8 mmol/kg) to mice

Page 17 12/17/07

10/539049 VALPROIC ACID ANALOGUES

caused minor motor damage, vs. severe damage, for Na valproate at 4.8 mmol/kg. 1 Na salt (500 mg) was dissolved in 2 mL saline to give an inflectable solution

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| FULL ESTIMATED COST | 50.76 | 224.78 |
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| CA SUBSCRIBER PRICE | -6.24 | -6.24 |

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FILE CONTAINS CURRENT INFORMATION. LAST RELOADED: Dec 14, 2007 (20071214/UP)

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(FILE 'HOME' ENTERED AT 15:27:50 ON 17 DEC 2007)

FILE 'REGISTRY' ENTERED AT 15:28:00 ON 17 DEC 2007 STRUCTURE UPLOADED 1

FILE 'STNGUIDE' ENTERED AT 15:28:51 ON 17 DEC 2007

'REGISTRY' ENTERED AT 15:32:17 ON 17 DBC 2007 STRUCTURE UPLOADED FILE

1 S L2 5 S L2 SSS FULL 222 FILE 'HCAPLUS' ENTERED AT 15:33:47 ON 17 DEC 2007

3 S L4 3 S ABBOTT, F7/AU AND KARAGIOZOV, S?/AU 3996 S VALPOCIC (A) ACID 2 S FLUORINATED (A) VALPROIC (A) ACID 2272

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This file contains CAS Registry Numbers for easy and accurate substance identification.

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0 "FLUORINE OR FLUORINATE OR FLUORINATED"

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0 "VPA OR VALPROIC (A) ACID" (S) "FLUORINE OR FLUORINATE OR FLUORINATE OR NATED"
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Page 19 12/17/07

10/539049 VALPROIC ACID ANALOGUES

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3 S ABBOTT, F?/AU AND KARAGIOZOV, S?/AU
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FILE 'STNGUIDE' ENTERED AT 15:38:46 ON 17 DEC 2007

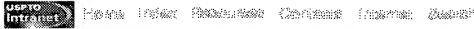
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Author (if known): Tang, Wei; Palaty, Jan; Abbott, Frank S.

Article or Chapter Title: Time course of .alpha -fluorinated valproic acid

Journal or Book Title: Journal of Pharmacology and Experimental Therapeutics

Volume and issue (for articles): 282(3),

Year of Publication: (1997), Page numbers: 1163-1172

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